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| NOVARTIS INSTITUTES FOR BIOMEDICAL RESEARCH, INC. 220 MASSACHUSETTS AVENUE CAMBRIDGE, MA 02139 | | | | |
| EXAMINER | | | | |
| NIEBAUER, RONALD T | | | | |
| ART UNIT | | PAPER NUMBER | | |
| 1654 | | | | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary

Application No.

10/594,413

Applicant(s)

PALERMO ET AL.

Examiner

RONALD NIEBAUER

Art Unit

1654

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 March 2011.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 21-24 and 26-38 is/are pending in the application.
- 4a) Of the above claim(s) 22-24, 26 and 30-38 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21 and 27-29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-946)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 3/15/11
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Applicants amendments and arguments filed on 3/15/11 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Previously, applicants elected group I and the species of compound as shown in example 45. Applicants elected species was found to be free of the prior art. However, no claim reads solely on the elected species. In accord with MPEP 803.02 the search was extended to the extent necessary to determine patentability of the Markush-type claim. As discussed in the 102 rejection art was found that reads on the Markush-type claim. In accord with MPEP 803.02 the search is not extended unnecessarily to all species.

Claims 1-20,25 have been cancelled.

Claims 22-23 are to a non-elected group.

Claims 22-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/3/11.

Claims 24,26, 30-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/3/11.

Claims 21,27-29 are under consideration.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 3/15/11 has been considered by the examiner.

Claim Rejections - 35 USC § 102

Applicants amendments have resulted in a different priority date for searching purposes of the instant claims. The reference below was cited in the previous office action. However, due to the change in priority the rejection is a new rejection necessitated by applicants amendments.

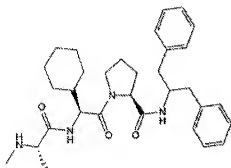
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 21,27-29 are rejected under 35 U.S.C. 102(a) as being anticipated by Sharma et al (WO 2004/005248, copy provided with office action dated 2/1/11).

Sharma teach IAP inhibitors (abstract). Sharma teach specific compounds including those in examples 10,15-16 (see pages 17-18). Sharma teach the compounds with carriers and in effective amounts (claim 7). In relation to the instant claims, example 16 of Sharma



meets the structural limitations of claims 27-29 since R1 is methyl, R2 is H, R3 is methyl, R4 is C6 cycloalkyl, R5 is H, R6,R6',R7,R7' are H, n is 0, Rd is Ar1-D-Ar2 where Ar1 is substituted phenyl (substituted with C(O)-NH-CH-CH2), D is C1 alkyl and Ar2 is phenyl. The configuration of the compound is such that Ar1 and Ar2 are attached as claimed. Since Sharma teach the compounds with carriers and in effective amounts (claim 7) the limitations of claim 21 are met.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

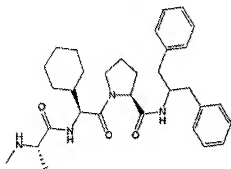
Claims 21,27-29 are rejected under 35 U.S.C. 102(e) as being anticipated by Sharma et al (WO 2004/005248, copy provided with office action dated 2/1/11).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C.

102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37

CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Sharma teach IAP inhibitors (abstract). Sharma teach specific compounds including those in examples 10,15-16 (see pages 17-18). Sharma teach the compounds with carriers and in effective amounts (claim 7). In relation to the instant claims, example 16 of Sharma



meets the structural limitations of claims 27-29 since R1 is methyl, R2 is H, R3 is methyl, R4 is C6 cycloalkyl, R5 is H, R6,R6',R7,R7' are H, n is 0, Rd is Ar1-D-Ar2 where Ar1 is substituted phenyl (substituted with C(O)-NH-CH-CH2), D is C1 alkyl and Ar2 is phenyl. The configuration of the compound is such that Ar1 and Ar2 are attached as claimed. Since Sharma teach the compounds with carriers and in effective amounts (claim 7) the limitations of claim 21 are met.

Response to Arguments 102

It is noted that this rejection is a new rejection necessitated by applicants amendments. Applicants arguments will be considered to the extent that they apply to the current rejection and claim set.

Applicants argue that they disagree with the interpretation of substituted phenyl and the assertion that the point of linkage can be by means of the substituent.

Applicants argue that the claims have been amended and that the interpretation of substituted phenyl is unreasonable.

Applicants argue that if applicants intended to claim compounds having an amide attached to a pyrrolidinyl ring then Ar1 would have to be an amide substituted with an aryl or het.

Applicants argue that the definition of benzene ring in the classification glossary shows that the Examiners interpretation is unreasonable.

Applicant's arguments filed 3/15/11 have been fully considered but they are not persuasive.

Although Applicants argue that they disagree with the interpretation of substituted phenyl and the assertion that the point of linkage can be by means of the substituent, it is noted that the instant specification expressly recites many substituents including alkyl and amino (page 9 last paragraph). The claims recite that Ar1 and Ar2 can be substituted phenyl. As discussed above Sharma teach compounds such that Ar1 is substituted phenyl (substituted with C(O)-NH-CH-CH₂), D is C1 alkyl and Ar2 is phenyl. Thus the interpretation of substituted phenyl is consistent with applicants own specification. With respect to the point of linkage it is noted that the instant claims do not specifically refer to a point of linkage. The claims do recite that Ar1 (and Ar2) 'is attached'. However, the phrase 'is attached' does not provide specifics about what portion is attached. Formula II shows (Rb)_n-Rd. Thus (Rb)_n is attached to Rd. There is no basis to limit 'is attached' to attachment at a specific location. Further, the phrase 'is attached' is open-ended and

could represent attachments via a linker or substituent for example. As claimed Rd is Ar1-D-Ar2. The hyphen (i.e. -) is used to represent a connection but such hyphen does not require that Ar1 is limited to only certain connections.

Although Applicants argue that the claims have been amended and that the interpretation of substituted phenyl is unreasonable, as discussed above the compound of Sharma reads on the claims as set forth above. MPEP 2111 states that: During patent examination, the pending claims must be “given their broadest reasonable interpretation consistent with the specification.” Since applicants own specification expressly recites many substituents including alkyl and amino (page 9 last paragraph) one would recognize that a substituted phenyl can include alkyl and amino groups. Thus the interpretation of substituted phenyl is consistent with applicants own specification. The claims do recite that Ar1 (and Ar2) ‘is attached’. However, the phrase ‘is attached’ does not provide specifics about what portion is attached. Further, the phrase ‘is attached’ is open-ended and could represent attachments via a linker for example. As claimed Rd is Ar1-D-Ar2. The hyphen (i.e. -) is used to represent a connection but such hyphen does not require that Ar1 is limited to only certain connections.

Although Applicants argue that if applicants intended to claim compounds having an amide attached to a pyrrolidinyl ring then Ar1 would have to be an amide substituted with an aryl or het, MPEP 2106 for example recites: Limitations appearing in the specification but not recited in the claim should not be read into the claim. *E-Pass Techs., Inc. v. 3Com Corp.*, 343 F.3d 1364, 1369, 67 USPQ2d 1947, 1950 (Fed. Cir. 2003) (claims must be interpreted “in view of the specification” without importing limitations from the specification into the claims unnecessarily). In the instant case, the specification and applicants intentions are not read into the

claims. If applicants 'intend' the claims to cover a certain scope then applicants should recite the claims accordingly.

Although Applicants argue that the definition of benzene ring in the classification glossary shows that the Examiners interpretation is unreasonable, it is first noted that the instant claims do not recite benzene nor does the instant specification use the definition as set forth in the classification system. As discussed above claims are given the broadest reasonable interpretation consistent with the specification. Further, the classification refers to 'bonded directly'. The instant claims recite 'is attached'. The phrase 'bonded directly' is not necessarily the equivalent of 'is attached'. Further, it is noted that there can be numerous classifications for any given invention. The IDS of 3/15/11 lists US 4,278,793. The cover page of such patent (section 51) lists 8 separate US classifications. Since applicants own specification expressly recites many substituents including alkyl and amino (page 9 last paragraph) one would recognize that a substituted phenyl can include alkyl and amino groups. Thus the interpretation of substituted phenyl is consistent with applicants own specification.

Claim Rejections - 35 USC § 103

Applicants amendments have resulted in a different priority date for searching purposes of the instant claims. A search for prior art with a 102b date with respect to 4/6/05 is separate from a search for prior art with a 102b date with respect to 4/7/04. Thus due to the change in priority the rejection below is a new rejection necessitated by applicants amendments.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 21,27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alnemri et al (US 2002/0160975) and Tachibana et al (EP 0115850, 08-84).

Alnemri teach peptides capable of binding to an inhibitor of apoptosis protein (abstract). Alnemri specifically teach (section 0215) peptides of sequence AVPFY (SEQ ID NO:23). Alnemri teach the use of such peptide in assays (section 0215, figure 20).

Alnemri does not expressly teach a peptide with R1 as recited in the instant claims.

Alnemri teach peptides capable of binding to an inhibitor of apoptosis protein (abstract). Alnemri specifically teach (section 0215) peptides of sequence AVPFY (SEQ ID NO:23). Alnemri teach the use of such peptide in assays (section 0215, figure 20) and administration of

the compositions (section 0170). Since Alnermi teach the use of the peptide for administration one would be motivated to use a stable version of the peptide. Tachibana teach that the methylation of an N-terminal amino group of a peptide depresses the hydrolysis of the N-terminal amino group by amino-peptidase (page 4 lines 18-21). One would have a reasonable expectation of success since Tachibana expressly teach that the methylation of an N-terminal amino group of a peptide depresses the hydrolysis of the N-terminal amino group by amino-peptidase (page 4 lines 18-21).

Upon methylation of the N-terminal amino group of the peptide of Alnermi the resulting peptide is of sequence (N-Me)AVPFY. Such peptide is of formula IV where R1 is methyl, R2 is H, R3 is C1alkyl, R4 is C3alkyl, U is of formula 2 with R6,R6',R7,R7',Rc,R5 being H, n is 0, Rd is Ar1-D-Ar2 (-C(O)-NH-CH(CH2-Ph)-C(O)-NH-CH(CH2-C6H4-OH)-C(O)-OH) is such that Ar1 is substituted phenyl (substituted with (-C(O)-NH-CH(CH2)-C(O)-NH-CH-C(O)-OH), D is C1 alkyl and Ar2 is substituted phenyl (substituted with -OH). The configuration of the compound is such that Ar1 and Ar2 are attached as claimed thus meeting the structural limitations of claims 27-29. Although Alnermi does not show stereochemistry one skilled in the art would be motivated to make the claimed compound, in the expectation that compounds similar in structure will have similar properties (see *In re Payne*, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979). See *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) and *In re Dillon*, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1991) and *MPEP* 2144.09 I,II). Since Alnermi teach the peptides with carriers (section 0046) and for administration one would be motivated to include the peptides as in claim 21 of the instant claims.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Double Patenting

The previous office action was mailed 2/1/11. The filing receipt for application 12992631 is dated 2/28/11. Thus this rejection is necessitated by applicants amendments.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting

ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 21,27-28 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-54 of copending Application No. 12/992631 (631). Although the conflicting claims are not identical, they are not patentably distinct from each other.

631 teach compounds of formula I (see claim 2) where R1 is C1alkyl, R2 is H, R3 is C1alkyl, R4 is C1alkyl, n is 0, A is het, D is O-C1alkyl (the O reads on substituted het such that D is alkyl in relation to the instant claims), and A1 is het. Thus 631 teach compounds of the formula in claim 27 of the instant claims. Although 631 does not show stereochemistry one skilled in the art would be motivated to make the claimed compound, in the expectation that compounds similar in structure will have similar properties (see *In re Payne*, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979). See *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) and *In re Dillon*, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1991) and MPEP 2144.09 I,II). Further, 631 teach various isomers (claim 2). 631 reach compositions comprising the compound (claim 7) thus one would be motivated to use carriers and effective amounts.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims are directed to an invention not patentably distinct from claims of commonly assigned 12/992631 as discussed above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned 12/992631, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Conclusion

Applicants amendments have resulted in a different priority date for searching purposes of the instant claims. The previous office action was mailed 2/1/11. The filing receipt for application 12992631 is dated 2/28/11. Thus rejections have been necessitated by applicants amendments.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ronald T Niebauer/
Examiner, Art Unit 1654

/Cecilia Tsang/

Supervisory Patent Examiner, Art Unit 1654